PATENT COOPERATION TREATY

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P58600B(WO)	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/01557	International filing date *(day/month/year)* 28.03.2003	Priority date *(day/month/year)* 28.03.2002
International Patent Classification (IPC) or both national classification and IPC A61M16/06		
Applicant OPTINOSE AS ET AL.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.10.2003	23.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Kroeders, M Telephone No. +31 70 340-1967

Form PCT/IPEA/409 (Cover Sheet) (January 2004)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/01557

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-25	as originally filed

Claims, Numbers

1-23	as originally filed
32-43	received on 19.12.2003 with letter of 19.12.2003
24-31	received on 26.04.2004 with letter of 26.04.2004

Drawings, Sheets

1/13-13/13	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 16-27, 31-34, 36, 37

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 16-27, 31-34, 36, 37

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15, 28-30, 35 38-43
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-15, 28-30, 35 38-43
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-15, 28-30, 35 38-43
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 16-27, 31-34, 36 and 37 were not searched in view of Article 17(2)(a)(i) PCT and Rule 39.1(iv) PCT and therefore no substantive examination can be performed. Moreover, claims 16-27, 31-34, 36 and 37 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated on the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention

This International Examining Authority found multiple (groups of) inventions in this international application, as follows:

Group 1: Claims: 1-15
A nasal delivery device comprising:
- A) first and second nosepiece units
- B) at least one substance supply unit
- C) a valve unit, for selectively supplying substance to the nosepiece units

Group 2: Claims: 28-30
A nasal delivery device comprising:
- F) a mouthpiece
- B) at least one delivery unit (considered to correspond to substance supply unit)
- D) a gas supply unit, for cycling a pressure to the nasal airway

Group 3: Claims: 35
A nasal delivery device comprising:
- F) a mouthpiece
- B) at least one delivery unit (considered to correspond to substance supply unit)
- E) a gas supply unit, for delivering and withdrawing a volume of gas

Group 4: Claims: 38-43
An interface member comprising:

A) at least one nosepiece

F) a mouthpiece

In order that an International Application may contain more than one invention, the inventions defined in the application must form "a group", namely they should be so linked, as to form a single general inventive concept (see Rule 13.1 PCT). This inventive concept finds expression in the independent claims according to the different inventions in terms of the same or corresponding special technical features. The definition "special technical features" refers to the features which, in the independent claims, involve an inventive step over the prior art.

In the present case the common or corresponding feature of independent claims 1 and 38 is A) at least one nosepiece. The common or corresponding feature of claims 1, 28 and 35 is B) at least one substance supply unit. The common or corresponding feature of claims 28, 35 and 38 is F) a mouthpiece. The common or corresponding features of claims 28 and 35 are B) at least one substance supply unit, and F) a mouthpiece. These features are disclosed in the documents cited in the search report and are therefore not only not involving an inventive concept over the prior art, but are not even new.
The remaining features of the independent claims, namely valve unit C), gas supply unit D) (supply of gas), gas supply unit E) (supply and removal of gas) and mouthpiece F) are different and have different purposes.

Therefore the application is considered to encompass four different, separate inventions, contrary to the requirements of Rule 13.1 PCT.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Document WO-A-01/78818, which is considered to represent the most relevant state of the art for independent claim 1, discloses (cf. page 16, line 5 to page 17, line 24):

a nasal device (110) for delivering a substance to a nasal airway of a subject, comprising:
first and second nosepiece units (183, 180), each including a nosepiece for fitting to respective nostrils of a subject;
at least one substance supply unit (page 16, line 10 to 12) for supplying substance for delivery to the nasal airway of the subject;

The subject-matter of claim 1 differs from this disclosure in that there is a valve unit for selectively fluidly connecting the at least one substance supply unit alternately to respective ones of the nosepiece units. In view of this difference, the subject-matter of claim 1 is new and meets the requirements of Article 33(2) PCT.

The differentiating feature mentioned above has the purpose of simplifying the delivery of substance to each of the subject's nostrils by eliminating the need to re-align the device with the subject. None of the available prior art documents describes the same feature for the same purpose.
Therefore, the subject-matter of claim 1 involves an inventive step and the claim meets the requirements of Article 33(3) PCT.

Document GB-A-408856 , which is considered to represent the most relevant state of the art for independent claim 28, discloses (cf. page 1, left column, lines 16 to 30):

a nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
a mouthpiece (9) through which a subject in use exhales;
at least one delivery unit (3) for delivering substance to a nasal airway of a subject on exhalation by the subject; and
a gas supply unit (patient) for applying a pressure in the nasal airway of the subject

The subject-matter of claim 28 differs from this disclosure in that the gas supply unit, upon activation by exhalation of the subject, triggers a cycling pressure.
In view of this difference, the subject-matter of claim 28 is new and meets the requirements of Article 33(2) PCT.

The differentiating feature mentioned above has the purpose of improving the delivery of substance to those nasal cavities of the subject that are more difficult to reach(e.g. paranasal sinuses, tuba auditiva and middle ears). None of the available prior art documents describes the same feature for the same purpose.
Therefore, the subject-matter of claim 28 involves an inventive step and the claim meets the requirements of Article 33(3) PCT.

Document GB-A-408856, which is considered to represent the most relevant state of the art for independent claim 35, discloses (cf. page 1, left column, lines 16 to 30):

> a nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
> a mouthpiece (9) through which a subject in use exhales;
> at least one delivery unit (3) for delivering substance to a nasal airway of the subject; and
> a gas supply unit (patient) for alternately delivering a volume of gas through the nasal airway of the subject

The subject-matter of claim 35 differs from this disclosure in that the gas supply unit is also suitable for withdrawing a volume of gas from the nasal airway of the subject. In view of this difference, the subject-matter of claim 35 is new and meets the requirements of Article 33(2) PCT.

The differentiating feature mentioned above has the purpose of causing the entrained substance to be flushed in alternate directions. None of the available prior art documents describes the same feature for the same purpose. Therefore, the subject-matter of claim 35 involves an inventive step and the claim meets the requirements of Article 33(3) PCT as well.

Document WO-A-00/51672 (cited in the application), which is considered to represent the most relevant state of the art for independent claim 38, discloses:

> a nasal delivery device, comprising, at least one nosepiece (30) for fitting to a

nostril of a subject and a mouthpiece (26) through which the subject in use exhales, wherein the mouthpiece (26) includes a flexible member (41) which is deflectable on exhalation into the mouthpiece (26)

The subject-matter of claim 38 differs from this disclosure in that the above mentioned features of the nasal delivery device form one interface member (the at least one nosepiece and mouthpiece form an integral element), which can be attached to the nasal delivery device.
In view of said difference, the subject-matter of claim 38 is new and meets the requirements of Article 33(2) PCT.

The differentiating feature mentioned above has the purpose of facilitating the exchange of the nosepiece(s) and mouthpiece, parts of which are contaminated in use by a previous subject. None of the available prior art documents describes the same feature for the same purpose. Eventhough the skilled person knows the importance of exchanging contaminated parts of a nasal delivery device, the exchange of all the contaminated parts as an integral component would not be considered obvious, due to the relative size and required complexity in design.
Therefore, the subject-matter of claim 38 involves an inventive step and the claim meets the requirements of Article 33(3) PCT.

The devices disclosed in claims 1, 28, 35 and 38 are industrial applicable and therefore the requirements of Article 33(4) PCT are met as well.

Claims 2-15, 29, 30 and 39-43 depend from independent claims 1, 28 and 38 and refer to further embodiments of the device described in these claims and thus meet the requirements of Articles 33(2), (3) and (4) PCT for the same reasons explained above.

24. The method of claim 22, wherein the flow resistor is a progressive resistor which provides a progressively increasing flow resistance to the gas flow.

25. The method of claim 24, wherein the progressive resistor comprises an expandable member which provides a progressively increasing resistance to the gas flow.

26. The method of any of claims 16 to 25, wherein substance is supplied from a single substance supply unit.

27. The method of any of claims 16 to 25, wherein substance is supplied to the first and second nosepiece units from respective ones of first and second substance supply units.

28. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
a mouthpiece through which a subject in use exhales;
at least one delivery unit for delivering substance to a nasal airway of the subject on exhalation by the subject; and
a gas supply unit for cycling a pressure in the nasal airway of the subject on exhalation by the subject.

29. The delivery device of claim 28, wherein the gas supply unit is configured to provide an alternating pressure in the nasal airway of the subject.

30. The delivery device of claim 28 or 29, wherein the gas supply unit is an exhalation breath actuatable unit which is fluidly connected to the mouthpiece such as to be actuated on exhalation by the subject.

31. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
delivering substance to a nasal airway of a subject; and
applying a varying pressure in the nasal airway of the subject.

32. The method of claim 31, wherein the step of applying a varying pressure in the nasal airway of the subject comprises the step of:
cycling the pressure in the nasal airway of the subject.

33. The method of claim 32, wherein the step of applying a varying pressure in the nasal airway of the subject comprises the step of:
alternating the pressure in the nasal airway of the subject.

34. The method of any of claims 31 to 33, further comprising the step of:
exhaling through a mouthpiece during delivery of substance.

35. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
a mouthpiece through which a subject in use exhales;
at least one delivery unit for delivering substance to a nasal airway of the subject; and
a gas supply unit for alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

36. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
delivering substance to a nasal airway of a subject; and
alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

37. The method of claim 36, further comprising the step of:
exhaling through a mouthpiece during delivery of substance.

38. An interface member for attachment to a nasal delivery device, comprising, as an integral element, at least one nosepiece for fitting to a nostril of a subject and a mouthpiece through which the subject in use exhales, wherein the mouthpiece

includes a flexible member which is deflectable on exhalation into the mouthpiece.

39. The interface member of claim 38, comprising first and second nosepieces for fitting to respective nostrils of a subject.

40. The interface member of claim 38 or 39, where being a disposable element.

41. The interface member of any of claims 38 to 40, wherein the mouthpiece comprises a tubular section through which the subject in use exhales.

42. The interface member of any of claims 38 to 40, wherein the mouthpiece comprises a cavity into which the subject in use exhales, with a part of the cavity being defined by the flexible member.

43. The interface member of any of claims 38 to 42, wherein the flexible member comprises a resilient member.